



06-16-04

1FW

Customer No.: 07178

Docket No.: 20199/100M275-US1

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of: Amedeo LEONARDI et al.

Serial No.: 10/768,953

Art Group: T.B.A.

Filed: January 29, 2004

Examiner: T.B.A.

For: **TREATMENT OF NEUROMUSCULAR DYSFUNCTION OF THE LOWER  
URINARY TRACT WITH SELECTIVE mGLU5 ANTAGONISTS**

June 14, 2004

**INFORMATION DISCLOSURE STATEMENT**

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

This Information Disclosure Statement is submitted in accordance with 37 C.F.R. §§1.97 and 1.98, and it is requested that the information set forth in this statement and in the listed documents be considered during the pendency of the above-identified application, and any other application relying on the filing date of the above-identified application or cross-referencing it as a related application.

1. This IDS should be considered, in accordance with 37 C.F.R. §1.97, as it is filed: (Check one of the boxes A-D)

- ☐ A. Within three months of the filing date of the above-identified national application or within three months of the entry into the national stage of the above-identified international application.
- ☒ B. Before the mailing date of a first office action on the merits, or a first office action after filing a request for continued examination.
- ☐ C. After (A) and (B) above, but before the mailing date of a final rejection, a notice of allowance, or any other action that closes prosecution, and Applicants have

made the necessary statement in box "i" below or paid the necessary fee in box "ii" below.

(check one of the boxes "i" and "ii" below:)

- ☐ i. Counsel states that, upon information and belief, each item of information listed herein was either (a) cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this IDS; or (b) was not cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of undersigned after making reasonable inquiry, was not known to any individual designated in §1.56(c) more than three months prior to the filing of this IDS.
- ☐ ii. A check for the fee set forth in §1.17(p), presently believed to be \$180, is enclosed.
- ☐ D. after (A), (B) and (C) above, but before payment of the issue fee: Counsel states that, upon information and belief, each item of information listed herein was either (i) cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the IDS; or (ii) was not cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of the undersigned after making reasonable inquiry, was not known to any individual designated in §1.56(c) more than three months prior to the filing of this IDS.
- ☐ i. A check for the fee set forth in §1.17 (p), presently believed to be \$180, is enclosed.

2. In accordance with 37 C.F.R. §1.98, this IDS includes a list (e.g., form PTO/SB/08a/b) of all patents, publications, or other information submitted for consideration by the office, either incorporated into this IDS or as an attachment hereto. A copy of each document listed is attached, except as explained below.

(check boxes A, B and/or C and fill in blanks, if appropriate.)

- ☒ A. Pursuant to the Notice issued by the United States Patent and Trademark Office dated July 11, 2003 waiving the requirements of 37 C.F.R. §1.98(a)(2)(i), a copy/copies of United States Patents and/or US Patent Publications on the attached PTO/SB/08a/b is/are not being submitted.
- ☐ B. Document(s) \_\_\_\_\_ is (are) deemed substantially cumulative to document(s) \_\_\_\_\_, and, in accordance with §1.98(c), only a copy of each of the latter documents is enclosed.
- ☐ C. Certain documents were previously cited by or submitted to the Office in the following prior applications, which are relied upon under 35 U.S.C. §120:

[SERIAL NO. & FILING DATE].



indicated for an item is taken from the face of the item and Applicant reserves the right to prove that the date of publication is in fact different.

7. CROSS REFERENCE UNDER 37 C.F.R. §1.78 TO RELATED APPLICATIONS

Pursuant to 37 C.F.R. §1.78, Applicant notes that the above-identified patent application may be related to the following U.S. Patent Applications:

(1) U.S. Patent Application Serial No \_\_\_\_\_, filed \_\_\_\_\_.

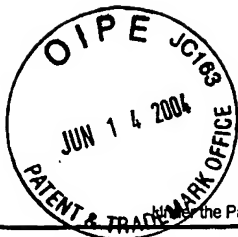
Early and favorable consideration is earnestly solicited.

Respectfully submitted,

Miss Beuster

**Mitchell Bernstein, Ph.D.**  
**Registration No. 46,550**  
**Agent for Applicant(s)**

**DARBY & DARBY P.C.**  
805 Third Avenue  
New York, N.Y. 10022  
(212) 527-7700 (phone)  
(212) 753-6237 (fax)



PTO/SB/08a/b (05-03)  
Approved for use through 05/31/2003. OMB 0651-0031  
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

<b>Substitute for form 1449/PTO</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	US 10/768,953
				Filing Date	Jan. 29, 2004
				First Named Inventor	Amedeo Leonardi
				Art Unit	To Be Assigned
				Examiner Name	To Be Assigned
Sheet	1	of	3	Attorney Docket Number	20199/100M275-US1

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code <sup>2</sup> (if known)			
	AA	US 5,462,942	10-31-1995	Hartog, et al.	
	AB	US 6,071,920	06-06-2000	Leonardi, et al.	
	AC	US 6,369,222 B1	04-09-2002	Binggeli, et al.	
	AD	US 2003/0162777	08-28-2003	Leonardi, et al.	
	AE	US 2003/0181446	09-25-2003	Leonardi, et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)				
	1.	WO 95/11891	05-04-1995	Astra Aktiebolag		
	2.	WO 99/02497	01-21-1999	Novartis-Erfindungen Verwaltungsgesellschaft mbh		
	3.	WO 99/06384	02-11-1999	Recordati S.A., Chemical and Pharmaceutical Company		
	4.	WO 00/63166	10-26-2000	F. Hoffmann-La Roche AG		
	5.	WO 00/69816	11-23-2000	Eli Lilly and Company		
	6.	WO 01/12627	02-22-2001	NPS Pharmaceuticals, Inc.		
	7.	WO 01/16121	03-08-2001	Merck & Co., Inc.		
	8.	WO 01/27070	04-19-2001	F. Hoffmann-La Roche		
	9.	WO 01/32632	05-10-2001	Eli Lilly and Company		
	10.	WO 02/46166	06-13-2002	F. Hoffmann-La Roche		
	11.	WO 02/062323	08-15-2002	Novartis AG		
	12.	WO 02/068417	09-06-2002	A. Slassi		
	13.	WO 02/092086	11-21-2002	F. Hoffmann-La Roche AG		
	14.	WO 02/094795	11-28-2002	F. Hoffmann-La Roche AG		

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the application number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	15.	Andersson K.E. (1988) "Current Concepts in the Treatment of Disorders of Micturition", <i>Drugs</i> , 35:477-494	
	16.	Carroll et al., (2001) "BAY36-7620: A Potent Non-Competitive mGlu1 Receptor Antagonist with Inverse Agonist Activity", <i>Molecular Pharmacology</i> , 59:965-973	
	17.	Cheng and Prusoff (1973) "Relationship between the inhibition constant (K <sub>i</sub> ) and the concentration of inhibitor which causes 50 per cent inhibition (I <sub>50</sub> ) of an enzymatic reaction", <i>Biochemical Pharmacology</i> , 22:3099-3108	

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--



PTO/SB/08a/b (05-03)  
Approved for use through 05/31/2003. OMB 0651-0031  
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Substitute for form 1449/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	US 10/768,953
				Filing Date	Jan. 29, 2004
				First Named Inventor	Amedeo Leonardi
				Art Unit	To Be Assigned
				Examiner Name	To Be Assigned
Sheet	2	of	3	Attorney Docket Number	20199/100M275-US1

18.	Corti et al., (1998) "Cloning and characterization of alternative mRNA forms for the rat metabotropic glutamate receptors mGluR7 and mGluR8", <i>European Journal of Neuroscience</i> , 10:3629-3641
19.	de Groat W. (1990) "Central neural control of the lower urinary tract", <i>Neurobiology of Incontinence</i> , Ciba Foundation Symposium, 151:27-56
20.	de Groat et al., (1993) "Neurophysiology of Micturition and Its Modification in Animal Models of Human Disease," <i>Nervous Control of the Urogenital System</i> , pg. 227-290
21.	De Lean et al., (1978) "Simultaneous analysis of families of sigmoidal curves: application to bioassay, radioligand assay, and physiological dose-response curves", <i>Amer. J. Physiol.</i> , 235:E97-E102
22.	Dray A. (1985) "The Rat Urinary Bladder", <i>Journal of Pharmacological Methods</i> , 13:157-165
23.	Gasparini et al. (1999) "2-Methyl-6-(phenylethynyl)-pyridine (MPEP), a potent, selective and systemically active mGlu5 receptor antagonist", <i>Neuropharmacology</i> , 38:1493-1503
24.	Goodman & Gillman, (1996) "Biotransformation of Drugs", <i>The Pharmacological Basis of Therapeutics</i> , 9 <sup>th</sup> Ed. McGraw-Hill, pg. 11-17
25.	Guarneri et al., (1991) "Effects of Different Drugs on the Cystometrogram in Conscious Rats", <i>Pharmacological Research</i> , 24:175-187
26.	Guarneri et al., (1993) "Effects of Drugs Used in the Therapy of Detrusor Hyperactivity on the Volume-Induced Contractions of the Rat Urinary Bladder", <i>Pharmacological Research</i> , 27:173-187
27.	Guarneri et al., (1994) "A review of flavoxate: pharmacology and mechanism of action", <i>Drugs of Today</i> , 30:91-98
28.	Hermans et al., (1999) "Effects of varying the expression level of recombinant human mGlu1α receptors on the pharmacological properties of agonists and antagonists", <i>British Journal of Pharmacology</i> , 126:873-882
29.	Hermans and Challiss (2001) "Structural, signalling and regulatory properties of the group I metabotropic glutamate receptors: prototypic family C G-protein-coupled receptors", <i>Biochem. J.</i> , 359:465-484
30.	Hinoi et al., (2001) "Characterization with [ <sup>3</sup> H]quisqualate of group I metabotropic glutamate receptor subtype in rat central and peripheral excitable tissues", <i>Neurochemistry International</i> , 38:277-285
31.	Hudtloff & Thomsen (1998) "Autoradiographic visualization of group III metabotropic glutamate receptors using [ <sup>3</sup> H]-L-2-amino-4-phosphonobutyrate", <i>British Journal of Pharmacology</i> , 124:971-977
32.	Johnson et al., (1999) "[ <sup>3</sup> H]-LY341495 as a novel antagonist radioligand for group II metabotropic glutamate (mGlu) receptors: characterization of binding to membranes of mGlu receptor subtype expressing cells", <i>Neuropharmacology</i> , 38:1519-1529
33.	Kingston et al. (1995) "Pharmacological analysis of 4-Carboxyphenylglycine Derivatives: Comparison of Effects on mGluRα and mGluR5α Subtypes", <i>Neuropharmacology</i> , 34:887-894
34.	Leonardi et al., (2001) "N-[2-[4-(2-Methoxyphenyl)-1-piperazinyl]ethyl]-N-(2-nitrophenyl) Cyclohexanecarboxamide: A Novel Pre- and Postsynaptic 5- Hydroxytryptamine1A Receptor Antagonist Active on the Lower Urinary Tract", <i>The Journal of Pharmacology and Experimental Therapeutics</i> , 299:1027-1037
35.	Lepor H. (1993) "Medical therapy for benign prostatic hyperplasia", <i>Urology</i> , 42:483-501
36.	Maggi et al., (1984) "Evidence for the Involvement of Arachidonic Acid Metabolites in Spontaneous and Drug-induced Contractions of Rat Urinary Bladder", <i>The Journal of</i>

Examiner Signature		Date Considered	
--------------------	--	-----------------	--



PTO/SB/08a/b (05-03)  
Approved for use through 05/31/2003. OMB 0651-0031  
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

<b>Substitute for form 1449/PTO</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	US 10/768,953
				Filing Date	Jan. 29, 2004
				First Named Inventor	Amedeo Leonardi
				Art Unit	To Be Assigned
				Examiner Name	To Be Assigned
Sheet	3	of	3	Attorney Docket Number	20199/100M275-US1

		<i>Pharmacology and Experimental Therapeutics</i> , 230:500-513	
37.	Maggi et al., (1986) "Somatovesical and Vesicovesical Excitatory Reflexes in Urethane-Anaesthetized Rats", <i>Brain Research</i> , 380:83-93		
38.	Malherbe et al., (1999) "Cloning and functional expression of alternative spliced variants of the human metabotropic glutamate receptor 8", <i>Molecular Brain Research</i> , 67:201-210		
39.	McGuire E. (1986) "Neuromuscular Dysfunction of the Lower Urinary Tract", <i>Campbell's Urology</i> , 1:616-638		
40.	Moroni et al., (1997) "Pharmacological Characterization of 1-Aminoindan-1,5-dicarboxylic Acid, a Potent mGluR1 Antagonist", <i>The Journal of Pharmacology and Experimental Therapeutics</i> , 281:721-729		
41.	Mutel et al., (2000) "Characterization of [ <sup>3</sup> H]Quisqualate Binding to Recombinant Rat Metabotropic Glutamate 1a and 5a Receptors and to Rat and Human Brain Sections", <i>Journal of Neurochemistry</i> , 75:2590-2601		
42.	Nilvebrant L. (2001) "Clinical experiences with tolterodine", <i>Life Sciences</i> , 68:2549-2556		
43.	Ruffmann R. (1988) "A Review of Flavoxate Hydrochloride in the Treatment of Urge Incontinence", <i>The Journal of International Medical Research</i> , 16:317-330		
44.	Spooren et al., (2001) "Novel allosteric antagonists shed light on mglu <sub>5</sub> receptors and CNS disorders", <i>TRENDS in Pharmacological Sciences</i> , 22:331-337		
45.	Thomsen et al., (1997) "Cloning and Characterization of a Metabotropic Glutamate Receptor, mGluR4b", <i>Neuropharmacology</i> , 36:21-30		
46.	Varney et al., (1999) "SIB-1757 and SIB-1893: Selective, Noncompetitive Antagonists of Metabotropic Glutamate Receptor Type 5", <i>The Journal of Pharmacology and Experimental Therapeutics</i> , 290:170-181		
47.	Wright et al., (2001) "[ <sup>3</sup> H]LY341495 Binding to Group II Metabotropic Glutamate Receptors in Rat Brain, <i>The Journal of Pharmacology and Experimental Therapeutics</i> , 298:453-460		

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>Applicant is to place a check mark here if English language Translation is attached.

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

Application No. (if known) 768,953

Attorney Docket No.: 20199/100M275-US1

# Certificate of Express Mailing Under 37 CFR 1.10

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mail, Airbill No. \_\_\_\_\_ in an envelope addressed to: \_\_\_\_\_

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Ev 418268399-us

on June 14, 2004  
Date

B.W. Fee

**Signature**

B. W. LEE

Typed or printed name of person signing Certificate

**Note:** Each paper must have its own certificate of mailing, or this certificate must identify each submitted paper.

Information Disclosure Statement (4 pages)  
PTO SB/08a/b (3 pages) and 47 References  
Return Receipt Postcard